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Appln. No. 10/691,333 Reply dated March 13, 2007 In response to February 12, 2007 Notice

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

(Currently amended) A compound of the formula

and pharmaceutically acceptable salts thereof;

wherein:

A is R'-C(O)-, wherein R' is selected from R'-

€,-C₆-alkyl;

or

each R^1 is independently selected from -C(0)-, $-S(0)_2$ -, -C(0)-C(0)-, -O-C(0)-, -O-C(0)-, -O-C(0)-, -O-C(0)-, $-NR^2$ -, $-NR^2$ -, $-NR^2$ -C(0)- or $-NR^2$ -C(0)-C(0)-;

each Ht is independently selected from C_3-C_7 cycloalkyl; C_5-C_7 cycloalkenyl; C_6-C_{14} aryl; or a 5-7 membered

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saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, $N(R^2)$, O, S and $S(O)_n$; wherein said aryl or said heterocycle is optionally fused to Q; and wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, -OR2, SR^{2} , $-R^{2}$, $-N(R^{3})(R^{3})$, $-R^{2}$ -OH, -CN, $-CO_{3}R^{3}$, $-C(O)-N(R^{2})_{2}$, $-S(O)_2-N(R^2)_2$, $-N(R^2)-C(O)-R^2$, $-N(R^2)-C(O)O-R^2$, $-C(O)-R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-Q$, methylenedioxy, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, $-NO_2$, Q, -OQ, $-OR^7$, $-SR^7$, $-R^7$, $-N(R^2)(R^7)$ or $-N(R^7)_2$; each R^2 is independently selected from H, or C_1 - C_4 alkyl optionally substituted with a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^{33})$; wherein any of said ring systems or $N(R^{33})$ is optionally substituted with 1 to 4 substituents independently selected from -X'-Y', -O-arylalkyl, -S-arylalkyl, $-N(Y')_2$, -N(H)-arylalkyl, $-N(C_1-C_4)$ alkyl)-arylalkyl, oxo. -O-(C_1 - C_4 alkyl), OH, C_1 - C_4 alkyl, -SO₂H, $-SO_{2} \cdot (C_{1} - C_{4} \text{ alkyl}) \;, \; -SO_{2} - NH_{2} \;, \; -SO_{2} - NH \; (C_{1} - C_{4} \text{ alkyl}) \;, \; -SO_{2} - N \; (C_{1} - C_{4} \text{ alkyl}) \;, \;$ $alkyl)_2$, $-NH_2$, $-NH(C_1-C_4 alkyl)$, $-N(C_1-C_4 alkyl)_2$, -NH-C(O)H, $-N(C_1-C_4 \text{ alkyl})-C(O)H$, $-NH-C(O)-C_1-C_4 \text{ alkyl}$, $-C_1-C_4 \text{ alkyl}-OH$, -OH, -CN, -C(O)OH, -C(O)O-C₁-C₄ alkyl, -C(O)-NH₂, $-C(0)-NH(C_1-C_4 \text{ alkyl})$, $-C(0)-N(C_1-C_4 \text{ alkyl})_2$, halo or $-CF_3$;

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X' is -0-, -S-, -NH-, -NHC(0)-, -NHC(0)0-, -NHSO₂-, or $-N(C_1-C_4)$ alkyl-;

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Y' is $C_1\text{-}C_{15}$ alkyl, $C_2\text{-}C_{15}$ alkenyl or alkynyl, wherein one to five carbon atoms in Y are optionally substituted with C_3 - C_7 cycloalkyl or C_5 - C_6 cycloalkenyl, C_6 - C_{14} aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and $S(O)_n$;

each \mathbb{R}^3 is independently selected from H, Ht, $C_1\text{-}C_6$ alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl or C_5 - C_6 cycloalkenyl; wherein any member of said R3, except H, is optionally substituted with one or more substituents selected from $-OR^2$, $-C(O)-N(R^2)_2$, $-S(O)_n-N(R^2)_2$, $-N(R^2)_2$, $-N(R^2)-C(O)O(R^2)$, $-N(R^2)-C(O)N(R^2)_2$, $-N(R^2)-C(O)-R^2$, Ht, -CN, $-SR^2$, $-C(O)OR^2$, $N(R^2) - C(0) - R^2;$

each R^{33} is selected from H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl or C_5 - C_6 cycloalkenyl, C_6 - C_{14} aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and $S(0)_n$;

each n is independently 1 or 2;

G, when present, is selected from H, R^7 or $C_1 - C_4$ alkyl, or, when G is C_1 - C_4 alkyl, G and R^7 are bound to one another either directly or through a C1-C3 linker to form a heterocyclic ring; or

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when G is not present (i.e., when x in $(G)_x$ is 0), then the nitrogen to which G is attached is bound directly to the R' group in -OR' with the concomitant displacement of one -ZM group from R7;

D is selected from $C_1\text{--}C_6$ alkyl which is substituted with Q, which is optionally substituted with one or more groups selected from C_3-C_6 cycloalkyl, $-R^3$, -0-Q or Q; C_2-C_4 alkenyl which is substituted with Q, which is optionally substituted with one or more groups selected from -QR2, -S-Ht, $-R^3$, -O-Q or Q; C_3-C_6 cycloalkyl, which is optionally substituted with or fused to Q; or C5-C6 cycloalkenyl, which is optionally substituted with or fused to Q;

each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; wherein Q contains one substituent selected from -OR2, -OR8, -O-arylalkyl, $-SR^8$, -S-arylalkyl, $-N(R^2)R^8$, $-N(R^2)$ -arylalkyl and may be optionally substituted with one or more additional substituents independently selected from oxo, -OR8, -O-arylalkyl -SR 8 , -S-arylalkyl, -N(R 2)R 8 , -N(R 2)-arylalkyl, $-OR^{2}$, $-R^{2}$, $-SO_{2}R^{2}$, $-SO_{2}-N(R^{2})_{2}$, $-N(R^{2})_{3}$, $-N(R^{2})-C(O)-R^{2}$, -OH, $(C_1 - C_4) - OH$, -CN, $-CO_2R^2$, $-C(O) - N(R^2)_2$, halo or $-CF_3$;

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each R^8 is independently selected from Ht, $-C_1-C_{15}$ branched or straight chain alkyl, alkenyl or alkynyl wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are independently replaced by W, or wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are substituted with Ht; and wherein R⁸ is additionally and optionally substituted with one or more groups independently selected from -OH, -S(C_1 - C_6 alkyl), -CN, -CF₃, -N(\mathbb{R}^2)₂, halo, -C₁-C₄-alkyl, -C₁-C₄-alkoxy; -Ht; -O-Ht; -NR²-CO-N(R²)₂; -CO-N(R²)₂; -R¹-C₂-C₆ alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C1-C4 alkoxy, Ht, -O-Ht, $[-NR^2-CO-N(R^2)_3$ or $-CO-N(R^2)_2$; or R^7 ;

wherein W is -0-, $-NR^2-$, -S-, -C(0)-, -C(S)-, $-C(=NR^2)-$, $-S(0)_{2}$, $-NR^{2}$ - $S(0)_{2}$, $-S(0)_{2}$ - NR^{2} -, $-NR^{2}$ - $C(0)_{2}$ -, -O- $C(0)_{1}$ NR²-, $-NR^{2}$ - $C(0)NR^{3}$ -, $-NR^{2}$ - $C(S)NR^{2}$ -, $-CONR^{2}$, $-NR^{2}C(0)$ -, $-C(S)NR^{2}$, $-NR^{2}C(S)$ -, $-NR^{2}-C(=N-CN)-NR^{2}-$, $-NR^{2}C(=N-CN)O-$ or -C(O)O-;

D' is selected from C_1 - C_{15} alkyl, C_1 - C_{15} alkoxy, C_2 - C_{15} alkenyl, C_2 - C_{15} alkenyloxy, C_2 - C_{15} alkynyl, or C_2 - C_{15} alkynyloxy, wherein D' optionally comprises one or more substituents independently selected from Ht, oxo, halo, -CF3, -OCF3, -NO2, azido, -SH, -SR³, -N(R³)-N(R³)₂, -O-N(R³)₂, -(R³)N-O-(R³), $-N(R^3)_2$, -CN, $-CO_2R^3$, $-C(O)-N(R^3)_2$, $-S(O)_n-N(R^3)_2$, $-N(R^3)-C(O)-R^3$, $-N(R^3)-C(O)-N(R^3)_2$, $-C(O)-R^3$, $-S(O)_n-R^3$, $-N(R^3)-S(O)_n(R^3)$, $-N(R^3) - S(O)_n - N(R^3)_2$, $-S - NR^3 - C(O)R^3$, $-C(S)N(R^3)_2$, $-C(S)R^3$,

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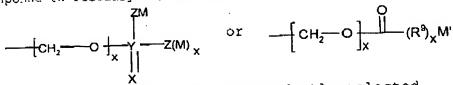
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 $-NR^3-C(O)OR^3$, $-O-C(O)OR^3$, $-O-C(O)N(R^3)_2$, $-NR^3-C(S)R^3$, =N-OH, $=N-OR^{3}$, $=N-N(R^{3})_{2}$, $=NR^{3}$, $=NNR^{3}C(O)N(R^{3})_{2}$, $=NNR^{3}C(O)OR^{3}$, $=NNR^{3}S(O)_{n}-N(R^{3})_{2}, -NR^{3}-C(S)OR^{3}, -NR^{3}-C(S)N(R^{3})_{2},$ $-NR^{3}-C[=N(R^{3})]-N(R^{3})_{2}, -N(R^{3})-C[=N-NO_{2}]-N(R^{3})_{2},$ $-N(R^3) - C[=N-NO_2] - OR^3$, $-OC(O)R^3$, $-OC(S)R^3$, $-OC(O)N(R^3)_2$, $-C(O)N(R^3)-N(R^3)_2$, $-N(R^3)-N(R^3)C(O)R^3$, $-N(R^3)-OC(O)R^3$, $-N(R^3) - OC(O)R^3$, $-N(R^3) - OC(O)R^3$, $-OC(S)N(R^3)_2$, $-OC(S)N(R^3)(R^3)$, or $-PO_3-R^3$:

E is selected from Ht; O-Ht; Ht-Ht; Ht fused with Ht; $-0-R^3$; $-N(R^2)(R^3)$; $-N(R^2)-Ht$; C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from R4 or Ht; C_2 - C_6 alkenyl, which is optionally substituted with one or more groups selected from R^4 or Ht; C_3-C_6 saturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht; or $C_5\text{--}C_6$ unsaturated carbocycle, which is optionally substituted with one or more groups selected from R4 or Ht;

each R^4 is independently selected from $-R^2$, $-OR^2$, $-OR^3$, $-SR^2$, $-SOR^2$, $-SO_2R^2$, $-CO_2R^2$, $-OC(O)-R^2$, $-C(O)-N(R^2)_2$, $-C(0) - NR^{2}(OR^{2})$, $-S(0)_{2} - N(R^{2})_{2}$, halo, $-NR^{2} - C(0) - R^{2}$, $-NR^{2} - OR^{2}$, $-N(R^2)_2$ or -CN;

each R' is independently selected from hydrogen,



wherein each M is independently selected from H, Li, Na, K, Mg, Ca, Ba, $-N(R^2)_4$, C_1-C_{12} -alkyl, C_2-C_{12} -alkenyl, or $-R^6$; wherein 1 to 4 $-CH_2$ radicals of the alkyl or alkenyl group, other than the $-CH_2$ that is bound to Z, is optionally replaced by a heteroatom group selected from O, S, S(O), S(O₂), or N(R²); and wherein any hydrogen in said alkyl, alkenyl or R⁶ is optionally replaced with a substituent selected from $O(R^2)$, $O(R^2)$

M' is H, C_1-C_{12} -alkyl, C_2-C_{12} -alkenyl, or $-R^6$; wherein 1 to 4 -CH₂ radicals of the alkyl or alkenyl group is optionally replaced by a heteroatom group selected from O, S, S(O), $S(O_2)$, or $N(R^2)$; and wherein any hydrogen in said alkyl, alkenyl or R^6 is optionally replaced with a substituent selected from $O(R^2)$, $O(R^2)$, O(

x is 0 or 1;

Z is O, S, $N(R^2)_2$, or, when M is not present, H;

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Y is P or S;

X is O or S; and

 R^9 is $C(R^2)_2$, O or $N(R^2)$; and wherein when Y is S, Z is not S; and

R⁶ is a 5-6 membered saturated, partially saturated or unsaturated carbocyclic or heterocyclic ring system, or an 8.10 membered saturated, partially saturated or unsaturated bicyclic ring system; wherein any of said heterocyclic ring systems contains one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; and wherein any of said ring systems optionally contains 1 to 4 substituents independently selected from -OH, -C₁-C₄ alkyl, -O-(C₁-C₄ alkyl) or -O-C(O)-(C₁-C₄ alkyl).

(Original) The compound according to claim 1, wherein R^8 is $-C_1-C_4$ -branched or straight chain alkyl, wherein one to two carbon atoms in said alkyl are independently replaced by W, wherein R^{B} is additionally and optionally substituted with one or more groups independently selected from -OH; $-C_1-C_4$ -alkoxy; -Ht; -O-Ht; $-NR^2-CO-N(R^2)_2$; -CO-N(R^2)₂; $-R^1-C_2-C_6$ alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C1-C4 alkoxy, Ht, -O-Ht, -NR²-CO-N(R²)₂ or -CO-N(R²)₂; or R⁷; wherein W is -O-, $-NR^2$ -, $-NR^2$ -S(O)₂-, $-NR^2$ -C(O)O-.

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 $- O-C(O) NR^2 - -NR^2 - C(O) NR^2 - , -NR^2 - C(S) NR^2 - , -NR^2 C(O) - , -C(=NR^2) - , \\ - C(O) NR^2 - , -NR^2 - C(=N-CN) - NR^2 - , -NR^2 C(=N-CN) O- or -C(O) O-; and \\ - wherein Ht, R^1, R^2 and R^7 are as defined in claim 1.$

3. (Previously presented) The compound according to claim 1, wherein R^8 is a $-C_1-C_4$ -branched or straight alkyl chain, wherein one to two carbon atoms are substituted with Ht;

wherein Ht is C_{6-14} aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, $N(R^2)$, O, S and $S(O)_n$, wherein any member of Ht is optionally substituted with one or more substituents independently selected from $O(N_1)$, $O(N_2)$, $O(N_2)$, $O(N_1)$, $O(N_1)$, $O(N_1)$, $O(N_2)$, $O(N_1)$,

4. (Currently amended) The compound according to claim 1, wherein \mathbb{R}^8 is selected from:

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(Original) The compound according to claim 1, wherein at least one R^7 is selected from:

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$$-CH_2-OSO_3Na_2$$
, $-CH_2-OSO_3(NH_4)_2$, O

acetyl, , , (L)-valine, -(L)-glutamic acid,

-(L)-aspartic acid, -(L)- γ -t-butyl-aspartic acid,

-(L)-(L)-3-pyridylalanine, -(L)-histidine, -CHO, CF3

$$\begin{array}{c} O \\ P \\ O \\ O \end{array}$$

$$\begin{array}{c} O \\ P \\ O \end{array}$$

 PO_3 -spermine, PO_3 -(spermidine)₂ or PO_3 -(meglamine)₂.

6. (Canceled).

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7. (Currently amended) The compound according to claim 1, wherein:

D' is -CH2-R'', wherein R'' is selected from:

isobutyl,;

wherein m is 0 to 3.

8. (Previously presented) The compound according to claim 1, wherein:

E is selected from:

$$NH_2$$
 NH_2 $NHMe$

9. (Currently amended) A compound having the

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formula (II):

and pharmaceutically acceptable salts thereof;

wherein:

A is selected from R'-C(0)-, wherein R' is selected from R1-C1-C6-alkyl,

each R1 is independently selected from -C(0)-, $-S(O)_{2}$, -C(O)-C(O), -O-C(O), $-O-S(O)_{2}$, $-NR^{2}$, $-NR^{2}$ - $S(O)_{2}$, $-NR^2-C(0) - or -NR^2-C(0)-C(0)$;

each Ht is independently selected from $C_3\text{-}C_7$ cycloalkyl; C_5-C_7 cycloalkenyl; C_6-C_{14} aryl; or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, $N(R^2)$, O, S and $S(O)_n$; wherein said aryl or said heterocycle is optionally fused to Q; and

wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, -OR2, SR^2 , $-R^2$, $-N(R^2)(R^2)$, $-R^2$ -OH, -CN, $-CO_2R^2$, -C(O)- $N(R^2)_2$, $-S(O)_{2}-N(R^{2})_{2}$, $-N(R^{2})-C(O)-R^{2}$, $-N(R^{2})-C(O)O-R^{2}$, $-C(O)-R^{2}$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-Q$, methylenedioxy, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, $-NO_2$, Q, -OQ, $-OR^7$, $-SR^7$, $-R^7$, $-N(R^2)(R^7)$ or $-N(R^7)_2$; each R^2 is independently selected from H, or $C_1 \text{-} C_4$ alkyl optionally substituted with a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(0)_n$ or $N(R^{33})$; wherein any of said ring systems or $N(R^{33})$ is optionally substituted with 1 to 4 substituents independently selected from -X'-Y', -O-arylalkyl, -S-arylalkyl, -N(Y')₂, -N(H)-arylalkyl, -N(C₁-C₄ alkyl)-arylalkyl, oxo, -O-(C_1 - C_4 alkyl), OH, C_1 - C_4 alkyl, -SO₂H, $-SO_{2}-\left(C_{1}-C_{4} \text{ alkyl}\right), \ -SO_{2}-NH_{2}, \ -SO_{2}-NH\left(C_{1}-C_{4} \text{ alkyl}\right), \ -SO_{2}-N\left(C_{1}-C_{4} \text{ alkyl}\right), \ -SO_{2}-N\left(C_{1}-C_{4} \text{ alkyl}\right)$ $alkyl)_2$, $-NH_3$, $-NH(C_1-C_4 \ alkyl)$, $-N(C_1-C_4 \ alkyl)_2$, -NH-C(O)H, $-N(C_1-C_4 \text{ alkyl})-C(0)H$, $-NH-C(0)-C_1-C_4 \text{ alkyl}$, $-C_1-C_4 \text{ alkyl}-OH$, -OH, -CN, -C(0)OH, -C(0)O- C_1 - C_4 alkyl, -C(0)- NH_2 , -C(O)-NH(C_1 - C_4 alkyl), -C(O)-N(C_1 - C_4 alkyl), halo or -CF₃; X' is -O-, -S-, -NH-, -NHC(O)-, -NHC(O)O-, -NHSO₂-,

or $-N(C_1-C_4)$ alkyl-; $Y' \text{ is } C_1-C_{15} \text{ alkyl}, C_2-C_{15} \text{ alkenyl or alkynyl, wherein}$

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one to five carbon atoms in Y are optionally substituted with C_3 - C_7 cycloalkyl or C_5 - C_6 cycloalkenyl, C_6 - C_{14} aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and S(O) $_n$;

each R^3 is independently selected from H, Ht, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl or C_5 - C_6 cycloalkenyl; wherein any member of said R^3 , except H, is optionally substituted with one or more substituents selected from $-OR^2$, $-C(O)-N(R^2)_2$, $-S(O)_0-N(R^2)_2$, $-N(R^2)_2$, $-N(R^2)-C(O)O(R^2)$, $-N(R^2)-C(O)N(R^2)_2$, $-N(R^2)-C(O)-R^2$; Ht, -CN, $-SR^2$, $-C(O)OR^2$, $N(R^2)-C(O)-R^2$;

each R^{33} is selected from H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl or C_5 - C_6 cycloalkenyl, C_6 - C_{14} aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and S(O)_n;

each n is independently 1 or 2;

each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; wherein Q contains one substituent selected from $-OR^2$, $-OR^8$, -O-arylalkyl, $-SR^8$, -S-arylalkyl, $-N(R^2)R^8$, $-N(R^2)-arylalkyl$ and

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may be optionally substituted with one or more additional substituents independently selected from oxo, $-OR^8$, $-O-arylalkyl <math>-SR^8$, -S-arylalkyl, $-N(R^2)R^8$, $-N(R^2)-arylalkyl$, $-OR^2$, $-R^2$, $-SO_2R^2$, $-SO_2-N(R^2)_2$, $-N(R^2)_2$, $-N(R^2)-C(O)-R^2$, -OH, $(C_1-C_4)-OH$, -CN, $-CO_2R^2$, $-C(O)-N(R^2)_2$, halo or $-CF_3$;

branched or straight chain alkyl, alkenyl or alkynyl wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are independently replaced by W, or wherein one to five carbon atoms in said alkyl, alkenyl are substituted with the said alkyl, alkenyl or alkynyl are substituted with the said wherein R^8 is additionally and optionally substituted with one or more groups independently selected from -OH, -S(C₁-C₆ alkyl), -CN, -CF₃, -N(R^2)₂, halo, -C₁-C₄-alkyl, -C₁-C₄-alkoxy; -Ht; -O-Ht; -NR²-CO-N(R^2)₂; -CO-N(R^2)₂; -R¹-C₂-C₆ alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C₁-C₄ alkoxy, Ht, -O-Ht, -NR²-CO-N(R^2)₂ or -CO-N(R^2)₂; or R^7 ;

wherein W is -O-, -NR²-, -S-, -C(O)-, -C(S)-, -C(=NR²)-, -S(O)₂-, -NR²-S(O)₂-, -S(O)₂-, -NR²-C(O)O-, -O-C(O)NR²-, -NR²-C(O)NR²-, -NR²-C(S)NR²-, -CONR², -NR²C(O)-, -C(S)NR², -NR²C(S)-, -NR²-C(=N-CN)-NR²-, -NR²C(=N-CN)O- or -C(O)O-;

D' is selected from C_1 - C_{15} alkyl, C_1 - C_{15} alkoxy, C_2 - C_{15} alkenyl, C_2 - C_{15} alkenyloxy, C_2 - C_{15} alkynyl, or C_2 - C_{15} alkynyloxy, wherein D' optionally comprises one or more substituents

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E is selected from Ht; O-Ht; Ht-Ht; Ht fused with Ht; $-O-R^3$; $-N(R^2)(R^3)$; $-N(R^2)-Ht$; C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from R^4 or Ht; C_2-C_6 alkenyl, which is optionally substituted with one or more groups selected from R^4 or Ht; C_3-C_6 saturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht; or C_5-C_6 unsaturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht; or C_5-C_6 unsaturated carbocycle, which is optionally substituted with one or more groups selected from R^4 or Ht;

each R^4 is independently selected from $-R^2$, $-OR^2$, $-OR^3$, $-SR^2$, $-SOR^2$, $-SO_2R^2$, $-CO_2R^2$, $-OC(O)-R^2$, $-C(O)-N(R^2)_2$,

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 $-C(0)-NR^{2}(OR^{2})$, $-S(0)_{2}-N(R^{2})_{2}$, halo, $-NR^{2}-C(0)-R^{2}$, $-NR^{2}-OR^{2}$, $-N(R^2)_2$ or -CN;

each \mathbb{R}^7 is independently selected from hydrogen,

$$\frac{Z^{M}}{\operatorname{CH}_{2}} = \frac{Z^{M}}{\operatorname{Z}(M)_{X}} \qquad \text{or} \qquad \left[\operatorname{CH}_{2} = \operatorname{O}\right]_{X}^{O} = \left(\operatorname{R}^{9}\right)_{X} M'$$

wherein each M is independently selected from H, Li, Na, K, Mg, Ca, Ba, $-N(R^2)_4$, $C_1-C_{12}-alkyl$, C_2 - C_{12} -alkenyl, or $-R^6$; wherein 1 to 4 - CH_2 radicals of the alkyl or alkenyl group, other than the $-CH_2$ that is bound to Z, is optionally replaced by a heteroatom group selected from O, S, S(O), S(O2), or N(R 2); and wherein any hydrogen in said alkyl, alkenyl or R^6 is optionally replaced with a substituent selected from oxo, $-C_1-C_4$ alkyl, $-N(R^2)_2$, $-N(R^2)_3$, -OH, $-O-(C_1-C_4)_3$ alkyl), -CN, $-C(O)OR^2$, $-C(O)-N(R^2)_2$, $S(O)_2-N(R^2)_2$, $-N(R^2)-C(O)-R_0$, $C(O)R^2$, $-S(O)_n-R^2$, $-OCF_3$, $-S(O)_n-R^6$, $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, or $-NO_2$;

M' is H, C_1-C_{12} -alkyl, C_2-C_{12} -alkenyl, or $-R^6$; wherein 1 to 4 $-CH_2$ radicals of the alkyl or alkenyl group is optionally replaced by a heteroatom group selected from O, S, S(O), $S(O_2)$, or $N(R^2)$; and wherein any hydrogen in said alkyl, alkenyl or R⁶ is optionally replaced with a substituent selected from oxo, $-OR^2$, $-C_1-C_4$ alkyl, $-N(R^2)_2$, $N(R^2)_3$, -OH,

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 $\begin{array}{l} -\text{O-}\left(C_{1}\text{-}C_{4} \text{ alkyl}\right), \ -\text{CN}, \ -\text{C}\left(\text{O}\right)\text{OR}^{2}, \ -\text{C}\left(\text{O}\right)\text{-}\text{N}\left(\text{R}^{2}\right)_{2}, \ -\text{S}\left(\text{O}\right)_{2}\text{-}\text{N}\left(\text{R}^{2}\right)_{2}, \\ -\text{N}\left(\text{R}^{2}\right)\text{-}\text{C}\left(\text{O}\right)\text{-}\text{R}_{2}, \ -\text{C}\left(\text{O}\right)\text{R}^{2}, \ -\text{S}\left(\text{O}\right)_{n}\text{-}\text{R}^{2}, \ -\text{OCF}_{3}, \ -\text{S}\left(\text{O}\right)_{n}\text{-}\text{R}^{6}, \end{array}$

 $-N(R^2)-S(O)_2(R^2)$, halo, $-CF_3$, or $-NO_2$;

x is 0 or 1;

Z is O, S, $N(R^2)_2$, or, when M is not present, H;

Y is P or S;

X is O or S; and

 R^9 is $C(R^2)_{\,2},\,\,O$ or $N(R^2)\,;$ and wherein when Y is S, Z is not S; and

 R^6 is a 5-6 membered saturated, partially saturated or unsaturated carbocyclic or heterocyclic ring system, or an 8-10 membered saturated, partially saturated or unsaturated bicyclic ring system; wherein any of said heterocyclic ring systems contains one or more heteroatoms selected from O, N, S, $S(O)_n$ or $N(R^2)$; and wherein any of said ring systems optionally contains 1 to 4 substituents independently selected from -OH, -C₁-C₄ alkyl, -O-(C₁-C₄ alkyl) or -O-C(O)-(C₁-C₄ alkyl).

10. (Original) The compound according to claim 9, wherein R⁸ is selected from:

ll. (Original) The compound according to claim 9, wherein \mathbb{R}^8 is selected from:

12. (Original) The compound according to claim 9,

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wherein R8 is selected from:

$$O_2N$$
 O_2
 O_2

13. (Original) The compound according to claim 9,

wherein R⁸ is selected from:

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(Currently amended) The compound according to 14. claim 9, wherein R is selected from:

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- (Currently amended) The compound according to 15. claim 9, wherein said compound is selected from compound numbers: 22, 24, 25, 26, 27, 31, 33, 35, 36, 38, 41, 43, 48, 49, 51, 52, 53, 54, 55, 56, 57, 59, 60, 69, 71, 72, 73, 74, 202, 203, 209, 213, 215, 223, 227, 231, 233, 236, 237, 239, 243, 247, 250, 260, 263, 271, 281, 289, 293, 295, 309, 317, 319, 320, 322, 334, 335, 348, 364, 367, 368, 375, 382, 383 and 396.
- (Currently amended) The compound according to claim 15, wherein said compound is selected from compound numbers: 26, 27, 31, 33, 35, 36, 38, 41, 43, 48, 49, 51, 52, 53, 54, 55, 56, 57, 59, 60, 69, 71, 72, 73, 74, 209, 215, 227, 233, 237, 281, 289, 295, 309, 322, 335, 364, 368, 382 and 383.
- (Previously presented) The compound according 17. to claim 16, wherein said compound is selected from: 54, 209, 237, 281, 295, 309, and 368.
- (Previously presented) A composition comprising 18. a compound according to claim 1 or 9, in an amount sufficient to inhibit an aspartyl protease; and a pharmaceutically acceptable carrier.

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- 19. (Original) The composition according to claim 18, wherein said composition is in a pharmaceutically acceptable form for administration to a human being.
- (Original) The composition according to claim 20. 18, wherein said composition additionally comprises an additional anti-viral agent.
- (Original) The composition according to claim 21. 18, wherein said composition comprises at least one additional therapeutic agent selected from (1 alpha, 2 beta, 3 alpha)-9-[2,3-bis(hydroxymethyl)cyclobutyl] - guanine [(-)BHCG, SQ-34514]; oxetanocin-G (3,4-bis-(hydroxymethyl)-2oxetanosyl]guanine); acyclic nucleosides, such as acyclovir, valaciclovir, famciclovir, ganciclovir or penciclovir; acyclic nucleoside phosphonates, such as (S)-1-(3-hydroxy-2phosphonyl-methoxypropyl)cytosine (HPMPC); ribonucleotide reductase inhibitors, such as 2-acetylpyridine 5-[(2chloroanilino)thiocarbonyl) thiocarbonohydrazone, 3'azido-3'deoxythymidine; other 2',3'-dideoxynucleosides such as 2',3'didcoxycytidine, 2',3'-dideoxyadenosine, 2',3'-dideoxyinosine, or 2',3'-didehydrothymidine; other aspartyl protease inhibitors, such as indinavir, ritonavir, nelfinavir, or [35-[3R*(1R*, 2S*)]]-[3[[(4-aminophenyl)sulfonyl](2-

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methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]tetrahydro-3-furanyl ester (amprenavir); oxathiolane nucleoside analogues, such as (-)-cis-1-(2-hydroxymethyl)-1,3oxathiolane 5-yl)-cytosine (lamivudine) or cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC); 3'-deoxy-3'-fluorothymidine; 5-chloro-2',3'-dideoxy-3'fluorouridine; (-)-cis-4-[2-amino-6-(cyclopropylamino)-9Hpurin-9-yl]-2-cyclopentene-1-methanol; ribavirin; 9-[4hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G); tat inhibitors, such as 7-chloro-5-(2-pyrryl)-3H-1,4benzodiazepin-2-(H) one (Ro5-3335) or 7-chloro-1,3-dihydro-5-(1H-pyrrol-2yl)-3H-1,4-benzodiazepin-2-amine (Ro24-7429); interferons, such as α -interferon; renal excretion inhibitors such as probenecid; nucleoside transport inhibitors such as dipyridamole; pentoxifylline; N-acetylcysteine (NAC); Procysteine; α -trichosanthin; phosphonoformic acid; immunomodulators, such as interleukin II or thymosin; granulocyte macrophage colony stimulating factors; erythropoetin; soluble CD4 and genetically engineered derivatives thereof; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as nevirapine (BI-RG-587), loviride $(\alpha$ -APA) or delavuridine (BHAP); phosphonoformic acid; 1,4dihydro-2H-3,1-benzoxazin-2-ones NNRTIs, such as (-)-6-chloro-

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4-cyclopropylethynyl-4-trifluoromethyl-1,4-dihydro-2H-3,1benzoxazin-2-one (L-743,726 or DMP-266); or quinoxaline NNRTIS, such as isopropyl (2S)-7-fluoro-3,4-dihydro-2-ethyl-3oxo-1(2H)-quinoxalinecarboxylate (HBY1293).

- (Previously presented) The composition 22. according to claim 18, wherein said composition is in an orally available dosage form.
- (Withdrawn) A method of treating a patient 23. infected with a virus that depends upon an aspartyl protease for an obligatory event in its life cycle comprising the step of administering to said patient a composition according to claim 18.
- (Withdrawn) A method of treating a patient infected with HIV-I or HIV-II comprising the step of administering to said patient a composition according to claim 18.
- (Withdrawn) The method according to claim 23, 25. comprising the additional step of administering to said patient an additional therapeutic agent selected from (1 alpha, 2 beta, 3 alpha)-9-[2,3-bis(hydroxymethyl)

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cyclobutyl]guanine [(-)BHCG, SQ-34514]; oxetanocin-G (3,4-bis-(hydroxymethyl) -2-oxetanosyl] guanine); acyclic nucleosides, such as acyclovir, valaciclovir, famciclovir, ganciclovir or penciclovir; acyclic nucleoside phosphonates, such as (S)-1-(3-hydroxy-2-phosphonyl-methoxypropyl)cytosine (HPMPC); ribonucleotide reductase inhibitors, such as 2-acetylpyridine 5-[(2-chloroanilino)thiocarbonyl) thiocarbonohydrazone, 3'azido-3'-deoxythymidine; other 2',3'-dideoxynucleosides such as 2',3'-dideoxycytidine, 2',3'-dideoxyadenosine, 2',3'dideoxyinosine, or 2',3'-didehydrothymidine; other aspartyl protease inhibitors, such as indinavir, ritonavir, nelfinavir, or [3S-[3R*(1R*, 2S*)]]-[3[[(4-aminophenyl)sulfonyl](2methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]tetrahydro-3-furanyl ester (amprenavir); oxathiolane nucleoside analogues, such as (-)-cis-1-(2-hydroxymethyl)-1,3oxathiolane 5-yl)-cytosine (lamivudine) or cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC); 3'-deoxy-3'-fluorothymidine; 5-chloro-2',3'-dideoxy-3'fluorouridine; (-)-cis-4-[2-amino-6-(cyclopropylamino)-9Hpurin-9-yl]-2-cyclopentene-1-methanol; ribavirin; 9-[4hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G); tat inhibitors, such as 7-chloro-5-(2-pyrryl)-3H-1,4benzodiazepin-2-(H)one (Ro5-3335) or 7-chloro-1,3-dihydro-5-(1H-pyrrol-2yl)-3H-1,4-benzodiazepin-2-amine (Ro24-7429);

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interferons, such as α -interferon; renal excretion inhibitors such as probenecid; nucleoside transport inhibitors such as dipyridamole; pentoxifylline; N-acetylcysteine (NAC); Procysteine; α -trichosanthin; phosphonoformic acid; immunomodulators, such as interleukin II or thymosin; granulocyte macrophage colony stimulating factors; erythropoetin; soluble CD4 and genetically engineered derivatives thereof; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as nevirapine (BI-RG-587), loviride (lpha -APA) or delavuridine (BHAP); phosphonoformic acid; 1,4dihydro-2H-3,1-benzoxazin-2-ones NNRTIs, such as (-)-6-chloro-4-cyclopropylethynyl-4-trifluoromethyl-1,4-dihydro-2H-3,1benzoxazin-2-one (L-743,726 or DMP-266); or quinoxaline NNRTIs, such as isopropyl (2S)-7-fluoro-3,4-dihydro-2-ethyl-3oxo-1(2H)-quinoxalinecarboxylate (HBY1293), wherein said additional agent is administered to said patient as either a separate dosage form or as a single dosage form together with said compound.

26. (Withdrawn) A method of treating a patient diagnosed with AIDS; AIDS related complex (ARC); progressive generalized lymphadenopathy (PGL); Kaposi's sarcoma, thrombocytopenic purpura; AIDS-related neurological conditions

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such as AIDS dementia complex, multiple sclerosis or tropical paraperesis; anti-HIV antibody-positive conditions; or HIVpositive conditions, comprising the step of administering to said patient a composition according to claim 18.

(Withdrawn) The method according to claim 26, 27. comprising the additional step of administering to said patient an additional therapeutic agent selected from (1 alpha, 2 beta, 3 alpha)-9-[2,3-bis(hydroxymethyl) cyclobutyl]guanine [(-)BHCG, SQ-34514]; oxetanocin-G (3,4-bis-(hydroxymethyl) -2-oxetanosyl] guanine); acyclic nucleosides, such as acyclovir, valaciclovir, famciclovir, ganciclovir or penciclovir; acyclic nucleoside phosphonates, such as (S)-1-(3-hydroxy-2-phosphonyl-methoxypropyl)cytosine (HPMPC); ribonucleotide reductase inhibitors, such as 2-acetylpyridine 5-[(2-chloroanilino)thiocarbonyl) thiocarbonohydrazone, 3'azido-3'-deoxythymidine; other 2',3'-dideoxynucleosides such as 2',3'-dideoxycytidine, 2',3'-dideoxyadenosine, 2',3'dideoxyinosine, or 2',3'-didehydrothymidine; other aspartyl protease inhibitors, such as indinavir, ritonavir, nelfinavir, or [3S-[3R*(1R*, 2S*)]]-[3[[(4-aminophenyl)sulfonyl](2methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]tetrahydro-3-furanyl ester (amprenavir); oxathiolane nucleoside analogues, such as (-)-cis-1-(2-hydroxymethyl)-1,3-

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oxathiolane 5-yl)-cytosine (lamivudine) or cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC); 3'-deoxy-3'-fluorothymidine; 5-chloro-2',3'-dideoxy-3'fluorouridine; (-)-cis-4-[2-amino-6-(cyclopropylamino)-9Hpurin-9-y1]-2-cyclopentene-1-methanol; ribavirin; 9-[4hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G); tat inhibitors, such as 7-chloro-5-(2-pyrryl)-3H-1,4benzodiazepin-2-(H)one (Ro5-3335) or 7-chloro-1,3-dihydro-5-(1H-pyrrol-2yl)-3H-1,4-benzodiazepin-2-amine (Ro24-7429); interferons, such as a-interferon; renal excretion inhibitors such as probenecid; nucleoside transport inhibitors such as dipyridamole; pentoxifylline; N-acetylcysteine (NAC); Procysteine; α -trichosanthin; phosphonoformic acid; immunomodulators, such as interleukin II or thymosin; granulocyte macrophage colony stimulating factors; erythropoetin; soluble CD4 and genetically engineered derivatives thereof; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as nevirapine (BI-RG-587), loviride (α -APA) or delavuridine (BHAP); phosphonoformic acid; 1,4dihydro-2H-3,1-benzoxazin-2-ones NNRTIs, such as (-)-6-chloro-4-cyclopropylethynyl-4-trifluoromethyl-1,4-dihydro-2H-3,1benzoxazin-2-one (L-743,726 or DMP-266); or quinoxaline NNRTIS, such as isopropyl (2S)-7-fluoro-3,4-dihydro-2-ethyl-3-

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oxo-1(2H)-quinoxalinecarboxylate (HBY1293), wherein said additional agent is administered to said patient as either a separate dosage form or as a single dosage form together with said compound.

- 28. (Previously presented) The compound according to claim 15, wherein said compound is compound number 368.
- 29. (Previously presented) The composition according to claim 19, wherein said composition is in an orally available dosage form.
- 30. (Previously presented) The composition according to claim 20, wherein said composition is in an orally available dosage form.
- 31. (Previously presented) The composition according to claim 21, wherein said composition is in an orally available dosage form.
- 32. (Withdrawn) The method according to claim 24, comprising the additional step of administering to said patient an additional therapeutic agent selected from (1 alpha, 2 beta, 3 alpha)-9-[2,3-bis(hydroxymethyl)

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cyclobutyl]guanine [(-)BHCG, SQ-34514]; oxetanocin-G (3,4-bis-(hydroxymethyl)-2-oxetanosyl]guanine); acyclic nucleosides, such as acyclovir, valaciclovir, famciclovir, ganciclovir or penciclovir; acyclic nucleoside phosphonates, such as (S)-1-(3-hydroxy-2-phosphonyl-methoxypropyl)cytosine (HPMPC); ribonucleotide reductase inhibitors, such as 2-acetylpyridine 5-[(2-chloroanilino)thiocarbonyl) thiocarbonohydrazone, 3'azido-3'-deoxythymidine; other 2',3'-dideoxynucleosides such as 2',3'-dideoxycytidine, 2',3'-dideoxyadenosine, 2',3'dideoxyinosine, or 2',3'-didehydrothymidine; other aspartyl protease inhibitors, such as indinavir, ritonavir, nelfinavir, or [3S-[3R*(1R*, 2S*)]]-[3[[(4-aminophenyl)sulfonyl](2methylpropyl)amino]-2-hydroxy-1-(phenylmethyl)propyl]tetrahydro-3-furanyl ester (amprenavir); oxathiolane nucleoside analogues, such as (-)-cis-1-(2-hydroxymethyl)-1,3oxathiolane 5-yl)-cytosine (lamivudine) or cis-1-(2-(hydroxymethyl)-1,3-oxathiolan-5-yl)-5-fluorocytosine (FTC); 3'-deoxy-3'-fluorothymidine; 5-chloro-2',3'-dideoxy-3'fluorouridine; (-)-cis-4-[2-amino-6-(cyclopropylamino)-9Hpurin-9-yl]-2-cyclopentene-1-methanol; ribavirin; 9-[4hydroxy-2-(hydroxymethyl)but-1-yl]-guanine (H2G); tat inhibitors, such as 7-chloro-5-(2-pyrryl)-3H-1,4benzodiazepin-2-(H)one (Ro5-3335) or 7-chloro-1,3-dihydro-5-(lH-pyrrol-2yl)-3H-1,4-benzodiazepin-2-amine (Ro24-7429);

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interferons, such as α -interferon; renal excretion inhibitors such as probenecid; nucleoside transport inhibitors such as dipyridamole; pentoxifylline; N-acetylcysteine (NAC); Procysteine; α -trichosanthin; phosphonoformic acid; immunomodulators, such as interleukin II or thymosin; granulocyte macrophage colony stimulating factors; erythropoetin; soluble CD4 and genetically engineered derivatives thereof; non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as nevirapine (BI-RG-587), loviride $(\alpha$ -APA) or delavuridine (BHAP); phosphonoformic acid; 1,4dihydro-2H-3,1-benzoxazin-2-ones NNRTIs, such as (-)-6-chloro-4-cyclopropylethynyl-4-trifluoromethyl-1,4-dihydro-2H-3,1benzoxazin-2-one (L-743,726 or DMP-266); or quinoxaline NNRTIS, such as isopropyl (2S)-7-fluoro-3,4-dihydro-2-ethyl-3oxo-1(2H)-quinoxalinecarboxylate (HBY1293), wherein said additional agent is administered to said patient as either a separate dosage form or as a single dosage form together with said compound.

33. (New) A compound selected from compound numbers: 26, 27, 28, 29, 30, 31, 32, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 59, 60, 61, 62, 63, 71, 72, 73, 74, 75,

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